S2 Appendix: Vaccine effectiveness assumptions

Table A below lists the numbers of patients included in vaccine and placebo arms and the number of infections for the analysis of the vaccine effectiveness for two and three doses. The two dose analysis included only patients who received doses 1 and 2 (regardless of whether they received dose 3) but excluded those in the reactogenicity subset because these lacked follow-up between 0 and 6 months following the first dose.   For this analysis we used only the number of confirmed Hepatitis E infections occurring in these patients between months 1.5 and 6 following the first dose (after the patients received the second dose and before any had received the third dose). The three dose analysis included only patients who had received all three doses, and included Hepatitis E infections occurring in the follow-up period between 7 and 19 months following the first dose.

Posterior distribution for vaccine effectiveness after two and three doses were derived using source data from Zhu et al [23] using an approach corresponding to method E in Ewell[1]. The prior model assumed independent risks of infection in each arm that followed a Beta distribution

$$p(\omega) \propto \omega^{\alpha-1}(1-\omega)^{\beta-1}$$

where we took $\alpha = \beta = 1$ (which assigns each possible value for the risk an equal probability density). The posterior distributions for the risks of infection in each arm (which represent our uncertainty about these risks having observed the data) were derived assuming a binomial model for the observed data and using beta-binomial conjugacy. Thus if the data we have show that there were n people at risk in a particular arm, and c of these became infected, then the posterior distribution would be given by

$$p(\omega|\text{data}) \propto \omega^{\alpha+c-1}(1-\omega)^{\beta+n-c-1}.$$

If the risk of infection in the vaccine group is r_v and the risk of infection in the placebo group is r_p, then vaccine effectiveness is given by $100 \times (1 - r_v /r_p)$. We estimated the posterior distribution of this statistic by simulation using 100,000 samples from the posterior distributions of r_v and r_p (Fig A, below).

This analysis gives posterior means (and central 95% credible intervals) of 80.2% (16.4%, 99.6%) for two doses and 93.3% (74.3%, 99.8%) for 3.

Table A: Source data for vaccine estimates of vaccine efficacy (from Zhu et al[1]).

Two dose analysis	Placebo group	Vaccine group
Number of people included	50838	50919
Number of infections	5	0
Three dose analysis		
Number of people included	48663	48693
Number of infections	15	0

Fig A. Probability distributions for two and three dose vaccine efficacy

Posterior distribution of 2−dose vaccine efficacy

Posterior distribution of 3−dose vaccine efficacy
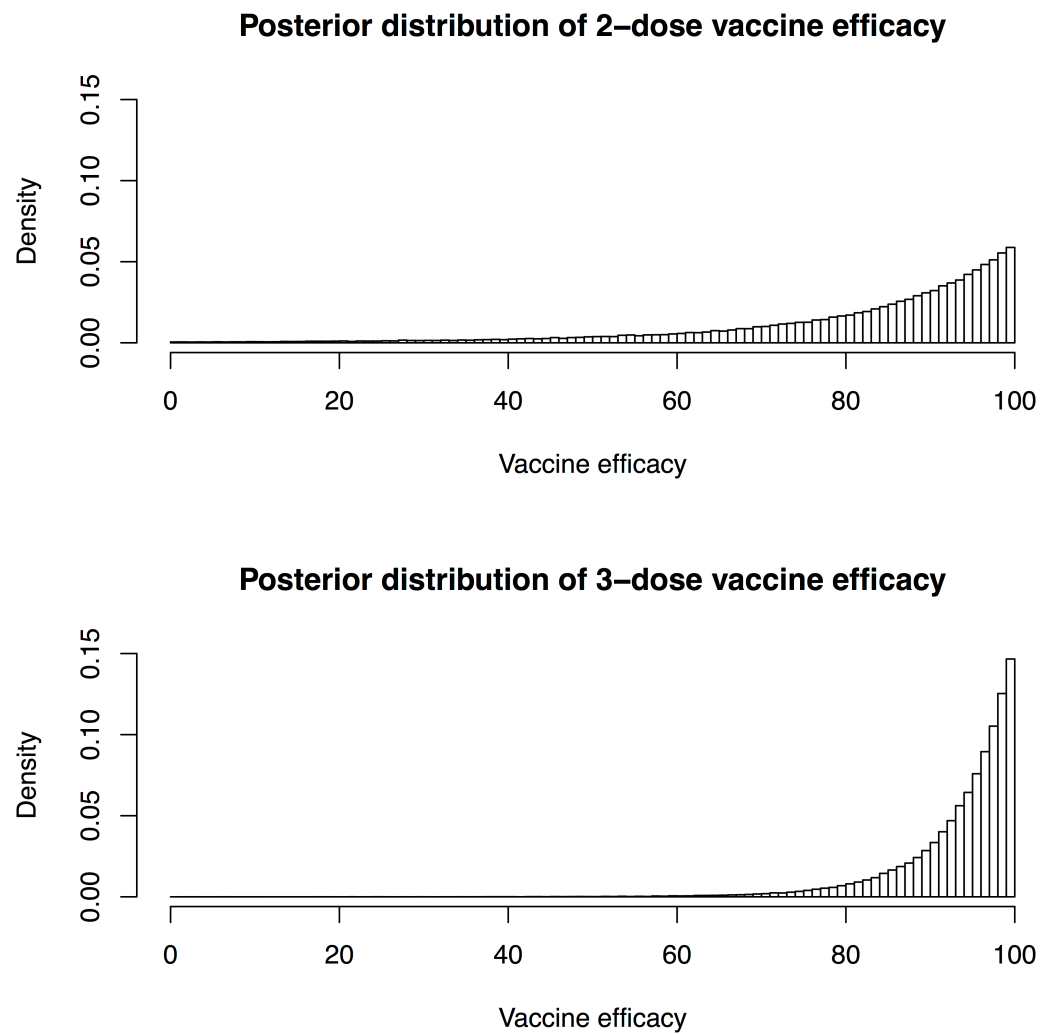
References:

[1] Ewell M. Comparing methods for calculating confidence intervals for vaccine efficacy. Stat Med.1996;15: 2379-2392.